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ANTHROPOLOGY.—PREHISTORIC CONTACT BETWEEN SOUTH AMERICA AND THE WEST INDIES

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The primary historical problem which has intrigued the archeologists of the Caribbean area has been that of the cultural relations between the West Indies and the two adjacent continents. A cultural connection with South America has for long been a generally accepted hypothesis, and more recently evidence has been increasing in support of the view that there were prehistoric contacts between the Greater Antilles and the United States[1] and Mexico.[2] In one case at least, hypothesis can now be set aside, for as a result of archeological work carried on during the past summer (1940), it is possible for the first time to link the West Indies with the South American mainland in an empirical manner which places the question of prehistoric contact beyond reasonable doubt. It is the purpose of this paper to indicate the nature of the evidence in support of this statement, and in a general way to correlate the newly discovered cognate mainland culture with the pattern of cultures previously recognized among the islands of the Caribbean.

A positive and provocative indication of direct contact appeared during the summer of 1933 when the writer, engaged in the Caribbean Archeological Program of the Yale Peabody Museum, found in the lowest stratum of a mound in the Lake Valencia region of Venezuela, a number of fragments of fine-grained, well-polished pottery with broadly incised lines and the so-called "doughnut eye." These specimens were absolutely atypical of the local culture and were described as trade sherds with West Indian affinities.[3]

In 1941, when the writer and Mr. George Howard of Yale University undertook an archeological survey of Venezuela, a culture was located on the lower Orinoco River which appeared to be the source of the trade sherds mentioned above.[4] Excavation in a site of this culture near the town of Barrancas produced fragmentary remains of a fine-grained pottery beautifully decorated with broadly incised curvilinear designs on lustrous

slips of red, black, yellow and brown. Outstanding among obvious features of the material were modeled *adornos* or ornamental heads of various animals which served as decorations for the sides of pots. A few days after the excavation at Barrancas was completed, the writer flew to Trinidad and had the pleasure of examining the material recently excavated by Mr. J. A. Bullbrook and Capt. J. E. L. Carter from the great shell midden at Erin Bay. This site is but a short distance across the Serpent's Mouth (as the intervening ocean channel is called) from the northern entrance to the Orinoco River, and only about 100 kilometers or 52 miles airline from the site at Barrancas. Some of the decorated pottery from the lower of the two strata at Erin Bay is to all appearances identical with that from the Orinoco River, and certainly such similarity exists as to rule out any likelihood of chance convergence in styles or even of sameness resulting only from casual contacts. As nearly as could be judged, numerous peculiar pieces from one site could be replaced by samples from the other without differences being readily detected. The similarity is further borne out by a comparison of the Barrancas material with that excavated at Erin Bay by Fewkes in the winter of 1912–1913 and illustrated in several of his papers.[5] Such is the present evidence for positive prehistoric contact between the West Indies and the South American mainland.

In order to correlate these connected cultures with the pattern of those recognized conditionally for the West Indies, we may first review the present theory regarding the population of the islands. From the linguistic and historical point of view, three major groups, the *Carib*, the *Arawak* and the *Ciboney*, appear to have occupied the Antilles in pre-Columbian times. These we shall consider in turn.

Carib. The most recent group in the West Indies is certainly the Carib, a people who are known historically to have raided and overrun most of the islands of the Lesser Antilles shortly before European contact.[6] Their South American origin is scarcely questioned but their culture, in terms of archeological remains, is very inadequately known. It may even be that any detailed knowledge of their culture is unobtainable, since the period of occupation by the Carib group possibly was too short to leave any accumulations sufficient for archeologists to interpret.

Arawak. The most widely spread of the major groups in the West Indies is the Arawak. Like the Carib, its presence is known from historic sources. Arawak occupation certainly antedated that of the Carib and is of larger duration, sufficiently long, indeed, so that it is not possible, on direct linguistic and historical evidence, to be certain that we are dealing with only a single group which, properly speaking, can be called Arawak. Rainey, working in Puerto Rico, described two cultures, an earlier Crab and a later Shell, which serve to distinguish phases of the Arawak group as I use the term here.[7] Although Rainey, with reasonable caution, did not

regard both cultures as Arawak, recent investigations by Rouse in Puerto Rico support this thesis.[8] In what is the most complete summary of West Indian archeology, Rainey went on to find widely spread evidences for his two cultures, identifying the Shell culture principally with the Greater Antilles and the Crab with the Lesser Antilles.[9] Regardless of revisions which may be made in his correlations, the existence of distinguishable earlier and later phases appears definitely established.

Ciboney. The third and most restricted of the major groups in the West Indies is the Ciboney which is best known from Cuba. Unlike the Carib and Arawak groups, the Ciboney people are not known from historical contacts but are referred to indirectly in the source literature. They clearly stand apart from the others, however, on archeological evidence, as they lacked pottery. Whenever they occupied the same territory as the Arawak (there is no evidence that the Ciboney and the protohistoric Carib ever shared the same islands), the Ciboney appear as the earlier group, which fact, however, by no means signifies that, in terms of actual time, they entered the West Indies before the Arawak. That the affinities of the Ciboney are with Florida is a widely proposed hypothesis[10] for which adequate empirical evidence, however, is yet to be established.

To return to the question of how the recently correlated sites of Barrancas, Venezuela and Erin Bay, Trinidad, fit into the general West Indian pattern, certain conclusions can be reached. From every point of view, the Erin Bay culture seems to belong to the Arawak group and it is the earlier phase of the remains which has direct ties with the Orinoco.[11] It is the feeling of some workers in Trinidad that this same phase correlates with the material at Cape Mayaro on the east coast of Trinidad which, we may note, has been described by Rainey as demonstrating a "remarkable similarity" with the Crab culture in Puerto Rico.[12] Thus it can be said that the Barrancas culture probably correlates with the early (Crab culture?) phase of the Arawak group in the West Indies.[13]

[1] Rouse, I., "Some Evidence Concerning the Origins of West Indian Pottery-Making," *Amer. Anth.*, **42**, 49–80 (1940).

[2] Ries, M., "Summary Report on the Tulane University-Cuban Navy Expedition to Cabo San Antonio, Cuba," Manuscript (1937).

[3] Osgood, C., "Excavations Near Lake Valencia, Venezuela," Manuscript (1935).

[4] This work was financed through the Institute of Andean Research by the Committee for Cultural and Commercial Relations with the Latin American Republics. It is expected that detailed results will appear in the *Yale University Publications in Anthropology* during 1942–1943.

[5] Fewkes, J. W., "Prehistoric Objects from a Shell-Heap at Erin Bay, Trinidad," *Amer. Anth.*, **16**, 200–220 (1914). Reprinted in *Contrib. from Heye Museum*, 1 (1915). The same illustrations are also available in Fewkes, J. W., "A Prehistoric Island Culture Area of America," *Bur. Amer. Ethnol.*, An. Rep. **34**, 70, plates 2–8 (1922).

[6] Loven, one of the principal writers on the prehistory of the West Indies but one who depends primarily on the historical sources, holds that the *Caribs* were in Trinidad

as well as the other small islands of the Lesser Antilles. In this view Bullbrook also concurs. Contrarily, Fewkes believes that the Caribs did not gain a foothold there, chiefly, it seems, because the typical stonework of the Lesser Antilles associated with the Caribs by Fewkes and other archeologists has not been found in Trinidad. There is a question, however, as to whether the stone artifacts referred to are actually Carib remains. In either event, there seems to be a sufficiency of historical evidence to demonstrate the reasonableness of Loven's theory. Loven, S., *Origins of the Tainan Culture, West Indies*, Göteborg, pp. 32–42 (1935); Bullbrook, J. A., "The Ierian Race," *Public Lectures . . . . of the Hist. Soc. of Trinidad and Tobago, 1938–1939* pp. 40–41 (1940); Fewkes, J. W., "A Prehistoric Island Culture Area of America," *Bur. Amer. Ethnol.*, An. Rep. **34**, 64–65 (1922).

[7] Rainey, F. G., "A New Prehistoric Culture in Puerto Rico," *Proc. Nat. Acad. Sci.*, **21**, 12–16 (1935).

[8] Rouse, I., "New Evidence Pertaining to Puerto Rican Prehistory," *Proc. Nat. Acad. Sci.*, **23**, 185 (1937). For a discussion of the evidence that these cultures are Arawak, see Rouse's section on the West Indies, soon to be published in the "Handbook of the South American Indians," *Bur. Amer. Ethnol.*, Washington, D. C.

[9] Rainey, F. G., "Scientific Survey of Porto Rico and the Virgin Islands," *New York Acad. Sci.*, **18**, part 1 (1940).

[10] Harrington, M. R., "Cuba Before Columbus," *Indian Notes and Monographs*, part 1, **2**, 423 (1921); Loven, S., *Origins of the Tainan Culture, West Indies*, Göteberg, p. 662 (1935).

[11] I am indebted to Capt. J. E. L. Carter for unpublished information on the distinctions between the upper and lower strata of the Erin Bay site.

[12] Rainey, F. G., "Scientific Survey of Porto Rico and the Virgin Islands," *New York Acad. Sci.*, **18**, part 1, 175 (1940).

[13] Our understanding of this problem will be greatly advanced by stratigraphic analyses of the Erin Bay and Barrancas deposits. The Trinidad research, it is hoped, will soon be furthered by coöperation between Trinidad archeologists and the Yale Peabody Museum.

GUANINE AND FACTOR Z_1, GROWTH SUBSTANCES FOR PHYCOMYCES

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Previous reports[1] have shown that the spore germination, early mycelial growth and gametic reproduction of *Phycomyces* at or near 25°C. in the presence of excess thiamin are markedly benefited by extracts from various natural products. By treatment with charcoal the natural extracts were separated into two fractions.[2] One of these, the Ca fraction, was the material adsorbed on charcoal from acid solution and eluted with ammoniacal acetone; the other, the D_R fraction, was the filtrate from the charcoal

treated extract. Both fractions were active but their effect when combined was more than additive. To account for the observed results two factors were assumed. One, factor Z_1, was assumed in the Ca fraction; the other, factor Z_2, in the D_R fraction.

Factor Z_1 was soluble in water, in aqueous alcohol and in aqueous acetone. It was thermostable to autoclaving. In electrodialysis it migrated to the cathode. It was widely distributed in natural products and was not identical with pyridoxine, lactoflavin, biotin, glutamine, pathothenic acid or para-amino-benzoic acid.[3]

The present paper is a progress report on further work with factor Z_1.

The presence of factor Z_1 was detected and the quantity present was approximated by determining the dry weight of the mycelium of *Phycomyces* produced in 72 hours at from 26° to 26.5°C. in the dark in a solution of minerals, sugar, asparagine and thiamin. To this basal solution preparations to be tested for Z_1 activity were added alone and in combination with a D_R fraction prepared from potato tubers.

We have confirmed the observation that factor Z_1 migrates to the cathode in electrodialysis. Our observations indicate that such migration occurs from solutions acid to about pH 5.0. Factor Z_1 was not destroyed by treatment with nitrous acid, but was destroyed by bromine and by hydrogen peroxide. Its activity was not eliminated by heating in saturated $Ba(OH)_2$ or in $4NH_2SO_4$ for 24 hours at 115°C. It was not precipitated by $Ba(OH)_2$ in methanol. It was soluble in 90 to 95 per cent ethanol. After electrodialysis it was still adsorbable on charcoal and elutable by ammoniacal acetone.

The effect of factor Z_1 was not obtained with the following mixture of vitamins or vitamin-like substances: glutamine, pimelic acid, vitamin K_1, lactoflavin, thiamin, ascorbic acid, *p*-amino benzoic acid, calcium pantothenate, nicotinamide and inositol. Oxyquinoline, urea, thiourea, thiazolidine-4-carboxylic acid and *d*-ribose were ineffective. A concentrate kindly supplied by W. H. Peterson containing a factor probably identical with folic acid of Williams was ineffective as a substitute for factor Z_1, at least after autoclaving. Choline, adenine, thymine, uracil, cytosine or xanthine was ineffective.

However, guanine in amounts of 0.1 μg. or more acted with the D_R fraction as the concentrates of factor Z_1 did. This is illustrated in table 1 where the results of 3 experiments with guanine alone and in combination with a D_R fraction from potato tubers are summarized. The D_R fraction contained 145.7 mg. of dry matter per ml. There is included in the table results with concentrates of factor Z_1. The concentrate of factor Z_1 for experiment 1 was prepared by saturating a Ca fraction from potato tuber tissue with $Ba(OH)_2$ and adding sufficient ethanol to make about 60% alcohol. After 48 hours at 4°C. the precipitate was removed and discarded. Sodium

nitrate was added to the filtrate which was acidified with H_2SO_4 to pH 3.0. After 4 hours at room temperature the solution was evaporated, saturated with $Ba(OH)_2$ and the precipitate removed. Excess barium was removed from the filtrate with H_2SO_4 and the solution adjusted to pH 6.0. This Z_1 concentrate contained 3.1 mg. of dry matter per ml. The concentrate used in experiments 2 and 3 also contained 3.1 mg. of dry matter per ml. It was prepared by acidifying a Ca fraction from potato tubers with phosphoric acid and treating with sodium nitrite overnight at room temperature. It was evaporated to small volume and alcohol added to precipitate the sodium phosphate. The precipitate was removed and the alcohol evaporated. The solution was saturated with $Ba(OH)_2$ and 2 volumes of methanol added. After standing overnight the precipitate was removed and the solution treated with sulfuric acid to remove excess barium.

TABLE 1

THE EFFECT OF GUANINE AND A CONCENTRATE OF FACTOR Z_1 ALONE AND IN COMBINATION WITH A D_R FRACTION (CONTAINING FACTOR Z_2) ON THE 72-HOUR GROWTH OF *Phycomyces* AT 26°C. IN A BASAL SOLUTION OF MINERALS, SUGAR, ASPARAGINE AND THIAMIN

ADDITIONS TO 25 ML. OF BASAL SOLUTION	DRY WEIGHT PER CULTURE OF *Phycomyces* MYCELIUM, MG. EXP. 1	EXP. 1 PLUS 0.1 ML. D_R FRACTION	EXP. 2	EXP. 2 PLUS 0.1 ML. D_R FRACTION	EXP. 3	EXP. 3 PLUS 0.1 ML. D_R FRACTION
100 μg. guanine	22.0	91.0	21.9	149.5	3.2	65.4
10 μg. guanine	22.0	83.0	10.9	143.0	2.2	54.6
1 μg. guanine	8.3	76.5	2.4	89.0	0.7	37.7
Nothing	4.2	67.7	1.2	52.7	Trace	20.1
1 ml. concentrate of factor Z_1	5.8	17.2	27.8	101.5	3.3	21.3
0.1 ml. concentrate of factor Z_1	9.2	79.5	6.1	111.0	1.1	44.3
0.01 ml. concentrate of factor Z_1	4.6	75.0	2.2	74.5	Trace	19.7

In experiment 1 the basal solution gave a yield of 8.2 mg. The addition of 1 μg. of guanine increased the weight to 16.6 mg. and 10 or 100 μg. were more effective. The addition of 0.1 ml. of the D_R fraction increased the weight to 135.5 mg. and combinations of guanine and the D_R fraction gave yields up to 182.0 mg. The Z_1 concentrate in experiment 1 was favorable although toxicity began to appear where 1 ml. was added per flask. Although in experiment 1 the yields in the solutions containing the D_R fraction were increased by the addition of guanine and by the two lower amounts of the Z_1 concentrate, in no instance were they significantly greater than the sum of the yields obtained with the D_R fraction alone and the guanine or factor Z_1 concentrate alone. In experiments 2 and 3 where the yields in the check solution were considerably less than in experiment 1, probably because of the condition of the spores used as inoculum, a more

marked action of guanine and of the factor Z_1 concentrate in the presence of the D_R fraction was evident.

Yeast nucleic acid was slightly effective and acid hydrolyzed nucleic acid gave effects approximately equal to the estimated guanine content.

Others have investigated pyrimidine and purine bases as growth substances for microörganisms. Richardson[4] found uracil to be a growth substance for *Staphylococcus aureus* under anaerobic conditions. Oxford, Lampen and Peterson[5] reported uracil, cytosine, guanine, adenine, xanthine and hypoxanthine ineffective with *Cl. acetobutylicum* as a substitute for the *BY* factor. Snell and Peterson[6] found choline, adenine, guanine, xanthine, hypoxanthine, uracil and cytosine ineffective as substitutes for an unidentified purine-like growth substance for *Lactobacillus casei*. Stockstad[7] reported for *Lactobacillus casei* a growth substance which appeared to be a dinucleotide containing guanine but no adenine. Guanine and thymine partially replaced it. Adenine, hypoxanthine and xanthine were as active as guanine. Uracil or cytosine did not replace thymine. Mueller and Miller[8] found adenine and Stockstad's dinucleotide essential for the growth of *Cl. tetani*. However, thymine and guanine were generally ineffective. Snell and Mitchell[9] state that each of the purine and pyrimidine bases of nucleic acid may, under certain conditions, become limiting factors for the growth of certain lactic acid bacteria. Adenine was found to stimulate the growth of *Lactobacillus arabinosus* and *L. pentosus* and to be essential for the growth of *Streptobacillus lactis*. Uracil stimulated the growth of *L. arabinosus* and of *L. mesenteroides*. Guanine was essential for the growth of *L. mesenteroides* and thymine for *S. lactis*. They state that in general the purine and pyrimidine bases were replaceable by the corresponding oxyderivatives. Hutchings, Bohonos, Hegsted, Elvehjem and Peterson[10] report evidence that a norit eluate factor believed to be the nucleotide of Stockstad is of importance in the nutrition of the chick. Guanine appears to have a higher degree of specificity for *Phycomyces* than for other organisms to which it has been reported to be of some significance.

Although guanine appears to be a growth factor for *Phycomyces* under the conditions of our experiments it is not factor Z_1. This follows because treatment with nitrous acid destroyed the activity of our sample of guanine while it did not affect that of factor Z_1 concentrates.

The relation of guanine to factor Z_1 is problematical. There are a number of possibilities among which the following may be mentioned. Factor Z_1 may be a derivative of guanine in which case both compounds may be active or one only may be active, the cell making the necessary transformation. If one only is active we have no evidence at present as to whether the active material is guanine or factor Z_1. In any event it seems that if factor Z_1 is a derivative of guanine there should be a substitution for at least one hydrogen in the amino group in the second position on the purine ring since

guanine was inactivated by treatment with nitrous acid while factor Z_1 was not. On the other hand guanine and factor Z_1 may be two distinct and unrelated compounds each of which is effective on the same cellular system. The relatively high degree of specificity of the known vitamins would militate against this assumption. Furthermore, guanine and factor Z_1 seem to have similar stabilities toward high temperature, acids, alkalies and oxidizing agents. They may, however, be unrelated substances which affect two distinct systems in the *Phycomyces* cell. Answers to these suppositions will probably have to wait the identification of factor Z_1 and its use in pure chemical form.

[1] Robbins, W. J., *Am. Jour. Bot.*, **26**, 772–778 (1939). Robbins, W. J., *Bot. Gaz.*, **101**, 428–429 (1939). Robbins, W. J., *Am. Jour. Bot.*, **27**, 559–564 (1940).

[2] Robbins, W. J., and Hamner, K. C., *Bot. Gaz.*, **101**, 912–927 (1940).

[3] Robbins, W. J., *Ibid.*, **102**, 520–535 (1940).

[4] Richardson, G. M., *Biochem. Jour.*, **30**, 2184 (1936).

[5] Oxford, A. E., Lampen, J. O., and Peterson, W. H., *Ibid.*, **34**, 1588–1597 (1940).

[6] Snell, E. E., and Peterson, W. H., *Jour. Bact.*, **39**, 273–285 (1940).

[7] Stockstad, E. L. R., *Jour. Biol. Chem.*, **139**, 475–476 (1941).

[8] Mueller, J. H., and Miller, P. A., *Ibid.*, **141**, 933–934 (1941).

[9] Snell, E. E., and Mitchell, H. K., *Proc. Nat. Acad. Sci.*, **27**, 1–6 (1941).

[10] Hutchings, B. L., Bohonos, N., Hegsted, D. M., Elvehjem, C. A., and Peterson, W. H., *Jour. Biol. Chem.*, **140**, 681–682 (1941).

RADIOACTIVE CARBON AS AN INDICATOR OF CARBON DIOXIDE UTILIZATION. VIII. THE RÔLE OF CARBON DIOXIDE IN CELLULAR METABOLISM

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I. Introduction.—Previous studies on the metabolism of non-chlorophyllous living systems in the presence of labeled CO_2 ($C^{11}O_2$ or $C^{13}O_2$) have shown that the organisms convert the labeled carbon into organic compounds which may occur as excreted end-products of metabolism, as cellular constituents or both. This phenomenon has been observed with *all* the systems thus far examined[1–12] (*Bacterium coli*, *Propionibacterium pentosaceum*, *Methanobacterium Omelianskii*, *Methanosarcina methanica*, *Clostridium acidi-urici*, *Streptococcus faecalis*, *Acetobacter* species, *Rhizopus nigricans*, *Rhizopus* species, *Aspergillus niger*, bakers yeast, Lebedev juice, barley roots, plants in the absence of light, rat liver and pigeon liver tissue).

In a few instances the utilization of CO_2 had been clearly demonstrated by methods not involving the use of labeled carbon. (Thus, the utilization of CO_2 by *Methanobacterium Omelianskii*, *Propionibacterium pentosaceum* and *Bacterium coli* had been established by the work of Barker,[13] of Wood and Werkman[14] and of Woods,[15] respectively. Also the reduction of CO_2 to CH_4 by *Methanosarcina methanica* had been predicted on the basis of theoretical considerations.[13] But in the majority of cases where the metabolic activities of the organism or tissue lead to the net production of CO_2, it is not possible to detect a small CO_2 uptake by ordinary chemical methods. Thus it remained for the tracer method to prove the well-nigh universal occurrence of CO_2 utilization.

For a number of years it has also been known that in the complete absence of CO_2, growth and metabolism of diverse living systems are seriously impaired. Under experimental conditions which would insure (1) the initial presence of not more than traces of CO_2, and (2) the prompt removal of additional amounts produced during metabolism, the germination of spores and growth of various microörganisms appeared to be greatly retarded, if not altogether prevented.[16–20] Even such respiratory activities, as methylene blue reduction by "resting cells," were shown to be similarly dependent upon the presence of CO_2.[21] But until now no attempt had been made to interpret these curious results.

The studies with labeled CO_2 have yielded data whose interpretation in terms of general biochemical mechanisms could be attempted. Hence it seemed desirable to investigate in how far such reactions could be of aid in elucidating the effects of CO_2 on growth and metabolism. Admittedly the ideas presented in this paper bear a somewhat speculative character. Nevertheless, they are capable of experimental verification, and may suggest new methods of approach to the many complicated and, at first sight apparently unrelated problems presented by living systems. In this connection may we quote G. N. Lewis[22] ". . . while the sort of vague surmise which is not based upon experimental evidence nor capable of experimental test has no place in our scientific method, rational speculation must always be regarded as the advance guard of experimental science."

II. The Possible Mechanisms of CO_2 Uptake by Living Systems.—One of the most important results of biochemical investigations of recent years has been the demonstration that enzyme-catalyzed processes are, in general, reversible. This implies that a reversal of those reactions in which CO_2 is liberated may be considered as possible mechanisms by which CO_2 is utilized and transformed into organic compounds. A striking example of such a process is furnished by the studies of Woods[15] on the formation of formic acid from CO_2 and H_2 by *B. coli*, in accordance with the equation:

$$HCOOH \rightleftarrows H_2 + CO_2 \qquad (1)$$

More frequently, however, CO_2 production by living organisms is ascribed to an enzymatic decomposition of keto-acids:

$$R\cdot CO\cdot COOH \rightarrow R\cdot CHO + CO_2 \qquad (2)$$

If this type of reaction were reversible, the utilization of CO_2 would then result in the formation of keto-acids[44] whose fundamental rôle and manifold vicissitudes in cellular metabolism have been firmly established.

Experiments reported in a previous communication have shown that the decarboxylation of $CH_3COCOOH$ by yeast carboxylase is indeed reversible.[7] Yet, the reverse reaction appeared to be much too slow to account for more than a very small fraction of the CO_2 uptake observed with living systems.

Investigations on CO_2 assimilation by propionic acid bacteria have suggested a similar, though not identical, method by which this compound is converted into organic substances.[3, 6, 9, 23] The available evidence strongly supports the following mechanism:

$$CO_2 + CH_3\cdot CO\cdot COOH \rightleftarrows COOH\cdot CH_2\cdot CO\cdot COOH^{24} \qquad (3)$$

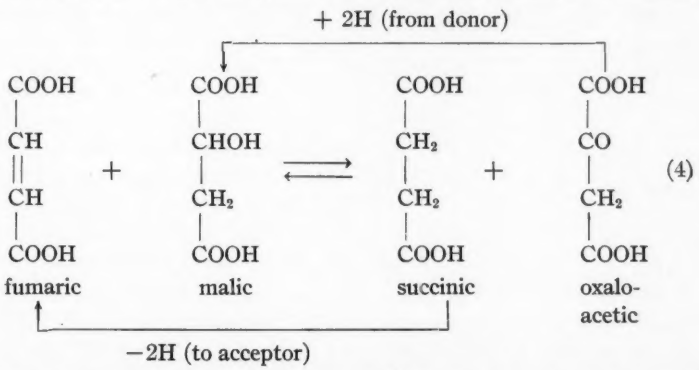
Normally, the oxaloacetic acid is reduced to succinic acid.

Furthermore, the occurrence of this reaction is apparently not limited to the propionic acid bacteria, on the contrary, it seems to be quite widespread. Various types of living systems have been shown to produce succinic and fumaric acids, at least in part, from CO_2. We refer to the work of Krebs and Eggleston with liver tissue,[25] of Smyth with *Staph. aureus*,[26] of Kleinzeller with yeast,[27] of Foster, *et al.*, with molds,[8] of van Niel, Ruben and Thomas with protozoa,[28] of Elsden[29] and of Werkman, *et al.*,[9] with *B. coli*.

It is particularly the general occurrence of a CO_2 fixation mechanism by which oxaloacetic acid and the closely related fumaric and succinic acids are formed which offers an opportunity for a simple interpretation of the above mentioned effects of CO_2 on growth and respiration. For the studies of Szent-Györgyi and co-workers,[30] as well as those of numerous investigators since, have revealed that this group of C_4-acids plays a fundamental rôle in cellular metabolism.

III. The Rôle of the C_4-Dicarboxylic Acids in Cellular Metabolism, and an Attempted Interpretation of the Necessity of CO_2 for Growth and Respiration.—According to our present knowledge in this field, it appears that the biological degradation of a substrate leads to a series of reactions in which electrons or hydrogen atoms are transferred to the ultimate acceptors by way of a rather extensive series of oxido-reduction reactions. In this chain of events, the reversible hydrogenation of oxaloacetate to malate, and of the latter (via fumarate) to succinate, plays the part of a catalytic hydrogen transporting system in various mammalian and avian tissues, as also in

microörganisms. Hence it has been proposed that the C_4-dicarboxylic acids comprise a "catalytic cycle," which can be represented as follows:



This hypothesis implies that the metabolic capacity of a system would depend in part upon the presence of sufficient amounts of the participating C_4-dicarboxylic acids. In growing cells the necessary increase in metabolic capacity must be brought about by a synthesis of one or more of the components of the catalytic cycle, and from the foregoing discussion it appears that such a synthesis can occur from CO_2 and pyruvic acid. If this were the only, or most important, way in which the C_4-dicarboxylic acids *originate*, it is obvious that CO_2 should be an indispensable component of the medium in which growth takes place.

However, these considerations apply rigorously only to conditions under which cell multiplication occurs. Yet, it has been shown by Hes[21] that even in suspensions of "resting cells," CO_2 is necessary for the normal functioning of the respiratory mechanism which results in methylene blue reduction. The explanation of this apparent anomaly becomes clear if one bears in mind the conditions under which Hes' experiments were conducted, in particular the presence of a strong CO_2-absorbing agent. The clue to an understanding of this phenomenon is furnished by the fact that oxaloacetate, apart from playing an important rôle in the Szent-Györgyi catalytic system, can as well undergo a number of other transformations. The most obvious of these is its decarboxylation. And, in the presence of a CO_2-absorbing reagent, this decomposition will proceed to such an extent that the supply of this biocatalyst will gradually disappear. Consequently, it can be asserted that *the decarboxylation of oxaloacetate constitutes a "leak" through which certain essential cell constituents are drained off*. The existence of a simple mechanism by which the components of this catalytic system can be replenished by the interaction of CO_2 and the ubiquitous intermediate product pyruvic acid, thus becomes of great importance as a means of "plugging" this leak.

Nor is the decarboxylation of oxaloacetate the only mode of its elimination from the cycle. From the studies of Knoop,[31] and particularly of Virtanen, *et al.*,[32] one may conclude that the synthesis of dicarboxylic amino acids takes place through a reaction between oxaloacetate or fumarate and ammonia or hydroxylamine. A further possibility for loss of the components of the catalytic cycle is provided by their ready diffusibility. In order to counteract losses by any of these processes, the C_4-dicarboxylic acid supply must therefore be constantly replenished.

Evans and Slotin[10] have recently shown that α-keto glutaric acid, produced by pigeon breast muscle in the presence of C^*O_2, contains radioactive carbon. In view of the work of Krebs and co-workers[33] it is possible to derive the ketoglutarate from oxaloacetate and pyruvate through the proposed citric acid mechanism. Also the recently reported formation of radioactive glycogen in the presence of C^*O_2 (Hastings, *et. al.*[34]) falls in line with the previous considerations. As these authors point out, the most likely interpretation of their experimental results is that the C^*O_2 is used in the synthesis of oxaloacetate. From this latter substance, radioactive pyruvic acid can be formed, which in turn leads to the formation of radioactive carbohydrate.

Whereas these contentions point to the fundamental rôle of a reaction by which oxaloacetic acid is synthesized from CO_2 and pyruvic acid, it does not necessarily follow that this reaction constitutes the only important function of CO_2 in metabolism. It has been emphasized on account of its obvious implications for general metabolism, and also because at the present time it represents one of the possible mechanisms for CO_2 utilization best supported by experimental evidence. Nevertheless, it must be realized that such a formation of oxaloacetate is no more than a special case of the introduction of CO_2 into a molecule by means of reversible decarboxylation.

IV. General Outlook on the Rôle of CO_2 in Biological Syntheses.—That the formation of oxaloacetate is not the only way by which CO_2 enters into cellular metabolism is clear from a consideration of the following well-established facts:

1. The reduction of CO_2 to formic acid by *B. coli* (Woods[15]).
2. The production of CH_4 from CO_2 in the methane fermentation (Barker, *et al.*[4, 13]).
3. The participation of CO_2 in the formation of acetic acid by *Clostridium aceticum* (Wieringa[35]) and by *Cl. acidi-urici* (Barker, *et al.*[5]).
4. The utilization of CO_2 in the formation of urea (Krebs and Henseleit,[36, 37] Evans and Slotin,[11] Rittenberg and Waelsch.[12]
5. The complete synthesis of cell constituents from CO_2 as the only carbon source by all autotrophic organisms.

Closely related to the autotrophic organisms, from the point of view of

synthesis of cellular materials from CO_2, are those microbes which can thrive in the presence of only a single one-carbon compound (CO, HCOOH, CH_3OH, CH_4). In these cases the carbon for all the widely divergent chemical constituents comprising the cell must of necessity be ultimately derived from "one-carbon building stones." If one further remembers that there are numerous cases of facultative autotrophism in which the organism can manufacture its cell constituents either completely from CO_2, or from some simple organic substance (to this class belong all the "hydrogen bacteria," and some "sulfur bacteria") it becomes tempting to suggest the possibility that even in the presence of an organic substrate, syntheses may occur in which CO_2 is one of the reactants. And in view of the fundamental similarity of the most diverse metabolic reactions,[38, 39] it then follows that such a possibility should also be seriously considered for the typically heterotrophic organisms.

The complex manner in which urea appears to be formed from NH_3 and CO_2, indicates that the CO_2 is initially built into a larger organic molecule (ornithine-citrulline-arginine cycle[11, 12, 36, 37]). In essence, this is somewhat similar to the above discussed mechanism for the formation of oxaloacetic acid, although not giving rise to a new carbon-carbon link. Furthermore, it is likely that also in the case of CO_2 reduction to formic acid, the CO_2 is first combined with an organic molecule, conceivably an enzyme, and that it is the reduction of this compound which results in the splitting off of HCOOH. The same reasoning can be applied to the formation of CH_4.

In a sense, therefore, these processes may be viewed as "syntheses of short duration." The formation of acetic acid from CO_2 and H_2 by *Cl. aceticum* furnishes an example in which the carbon atoms from two CO_2 molecules become permanently combined. Also the production of acetic acid by *Cl. acidi-urici* must involve such a synthesis since Barker, *et al.*, have shown that the decomposition of uric acid in the presence of C^*O_2 gives rise to acetic acid in which both carbon atoms are labeled.[5]

These last mentioned syntheses thus form a logical bridge to those processes in which large organic molecules are built up with the aid of CO_2. The step-wise elaboration of carbon compounds from such small elementary units would afford the most flexible mechanism for the synthesis of the endless variety of cellular constituents. Since many microörganisms are capable of effecting these syntheses starting with any one of a large number of simple carbon compounds,[†] it would seem entirely possible that at least for some of the syntheses CO_2 is used as a building stone. Otherwise it would be necessary to postulate the existence of a large variety of synthetic mechanisms for the elaboration of the same compounds.

So far this discussion has dealt with reactions in which CO_2 plays an important part, but which are independent of light. It has been deduced

from the available evidence that also in photosynthesis the actual CO_2 uptake and reduction can occur in the dark (see especially the striking demonstration by Gaffron that green algae can reduce CO_2 in darkness in the presence of H_2[41]) and that the light only serves to cause a photodecomposition of H_2O,[42] thus providing for a supply of reducing substances. This tends to link the process of photosynthesis directly to all other cases of biological utilization of CO_2.

We have, in the previous section, pointed out that the formation of oxaloacetic acid from CO_2 and pyruvic acid is but a special instance of a reversed decarboxylation reaction. In its most general formulation it can be represented by the equation:

$$RH + CO_2 \rightleftarrows RCOOH \qquad (5)$$

The very generality of this equation renders it perhaps the most adaptable mechanism for CO_2 utilization by living systems. It may well be that future work will demonstrate that the different cases of CO_2 reduction are but variants of this formulation. In this connection the experiments of Ruben, *et al.*, may be mentioned.[1, 43] These investigators allowed green algae to utilize C^*O_2 in the dark and found that the C* assimilated became lodged in a large molecule (molecular weight ~1000), and furthermore showed that a considerable portion of the C* was present in carboxyl groups. Equation (5) was proposed to account for their results.

The general inferences that can be drawn from the preceding considerations lead, we believe, to a unified concept of the rôle played by carbon dioxide in cellular metabolism.

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† E.g., den Dooren de Jong has demonstrated that *Pseudomonas putida* can be grown with any one of some 77 different organic compounds as the sole carbon source, including such diverse molecular species as: saturated and unsaturated fatty acids, hydroxy acids, dibasic and tribasic acids, alcohols, carbohydrates, amines, amino acids, amides, aromatic compounds, etc.[40]

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REPRESENTATION OF MEASURABLE FLOWS IN EUCLIDEAN 3-SPACE

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1. The purpose of this note is to show that every measurable flow defined on a measure space satisfying certain separability conditions is isomorphic to a continuous flow on a subset of a Euclidean 3-space with ordinary Lebesgue measure.

2. We begin with definitions.[1] A *measure space* $\Omega(\mathfrak{B}, m)$ is a system of a space Ω, a Borel field $\mathfrak{B}$ of subsets M of Ω, and a countably additive completed measure $m(M)$ defined on $\mathfrak{B}$ such that $0 < m(\Omega) < \infty$. A set belonging to $\mathfrak{B}$ is called *measurable*. A measure space $\Omega(\mathfrak{B}, m)$ is *properly separable* if there exists a countable collection $\mathfrak{A}$ of measurable sets, called a *basis*, such that, for any $M \in \mathfrak{B}$ and for any $\epsilon > 0$, there exists a subsequence $\{M_n\}$ $(n = 1, 2, \ldots)$ from $\mathfrak{A}$ such that $M \subset \sum_{n=1}^{\infty} M_n$ and $\sum_{n=1}^{\infty} m(M_n) < m(M) + \epsilon$. A countable collection $\mathfrak{A}$ of subsets of Ω is a *separating sequence* of Ω if, for any two distinct points of Ω, there exists at least one set from $\mathfrak{A}$ which contains one but not both of them.

If Ω is a Lebesgue measurable subset of a Euclidean n-space R^n with a finite Lebesgue measure, and if $\mathfrak{L}(\Omega)$ is the collection of all Lebesgue measurable subsets of Ω, then $\Omega(\mathfrak{L}(\Omega), \mu)$ (μ means n-dimensional Lebesgue measure in R^n) is called a *Lebesgue measure space*. More generally, if Ω is an arbitrary subset of a Euclidean n-space R^n with a finite Lebesgue outer measure, and if $\mathfrak{L}^*(\Omega)$ is the collection of all subsets M of Ω of the form: $M = \Omega \cdot \Lambda$, where Λ is a Lebesgue measurable set of R^n, then $\Omega(\mathfrak{L}^*(\Omega), \mu^*)$ (μ^* means n-dimensional Lebesgue outer measure in R^n) is called a *Lebesgue* measure space*.[2] Clearly, Lebesgue and Lebesgue* measure spaces are properly separable and have a separating sequence of measurable sets.

A *measure preserving transformation* (of a measure space onto another or onto the same measure space), a *flow* (= one parameter group of measure preserving transformations of a measure space onto itself), and the notions of *invariant sets* and *ergodicity* are defined as usual. A flow $\{T_t\}$ $(-\infty < t < +\infty)$ defined on a measure space $\Omega(\mathfrak{B}, m)$ is *measurable* if, for any $M \in \mathfrak{B}$, the set $\overline{M} = [(\omega, t) : T_t(\omega) \in M]$ is measurable in the product space of Ω with the real t-axis, where measure is defined multiplicatively in terms of the given measure $m(M)$ on Ω and the Lebesgue measure on t-axis. Two flows $\{S_t\}$ and $\{T_t\}$ defined on two measure spaces $\Omega(\mathfrak{B}, m)$ and $\Omega'(\mathfrak{B}', m')$, respectively, are *isomorphic* to each other if it is possible to find two in-

variant sets of measure zero $N \in \mathfrak{B}$, $N' \in \mathfrak{B}'$ and a measure preserving transformation of $\Omega - N$ onto $\Omega' - N'$ which carries $\{S_t\}$ into $\{T_t\}$.

3. Our main results are:

THEOREM 1. *Let $\{T_t\}$ be a measurable flow defined on a properly separable measure space having a separating sequence of measurable sets. If every point of the space is of measure zero, then $\{T_t\}$ is isomorphic to a continuous flow on a Lebesgue* measure space in a Euclidean 3-space R.*[3]

THEOREM 2. *Every measurable flow defined on a Lebesgue measure space in R^n $(n \geqq 1)$ is isomorphic to a continuous flow on a Lebesgue measure space in R^3.*

It is desirable to represent $\{T_t\}$ as a differentiable or an analytic flow in R^3. But this is not always possible. For instance, if $\{T_t\}$ is a group of rotations of a circumference (with one-dimensional Lebesgue measure), then the corresponding representation space in R^3 must be a simple Jordan curve with a positive three-dimensional Lebesgue measure. It is, however, easy to see that such a curve cannot be differentiable. The proof of Theorem 1 will be given in sections 5, 6 and 7, and Theorem 2 will be proved in section 6.

4. Let $\Omega(\mathfrak{B}, m)$ be a measure space, and let S be a measure preserving transformation of $\Omega(\mathfrak{B}, m)$ onto itself. Let further $f(\omega)$ be a positive valued measurable and integrable function defined on Ω. We assume that there exists a constant $c > 0$ such that $f(\omega) \geqq c$ for all $\omega \in \Omega$. Consider the product space of Ω with the real u-axis, with the measure $\overline{m}(\overline{M})$ defined on it multiplicatively in terms of the measure $m(M)$ on Ω and the Lebesgue measure on the u-axis. Let $\bar{\Omega}$ be the portion of this product space under the graph of $f(\omega)$, i.e. the set of all points of the form $\bar{\omega} = (\omega, u)$, $\omega \in \Omega$, $0 \leqq u < f(\omega)$, and let $\overline{\mathfrak{B}}$ be the collection of all $\overline{m}$-measurable subsets $\overline{M}$ of $\bar{\Omega}$. Then $\bar{\Omega}(\overline{\mathfrak{B}}, \overline{m})$ is a measure space and the flow $\{T_t\}$ defined on it by[3]

$$
\begin{aligned}
T_t(\omega, u) &= (\omega, u + t), \text{ if } -u \leqq t < -u + f(\omega), \\
&= (S^n(\omega), u + t - f(\omega) - \ldots - f(S^{n-1}(\omega))), \\
&\quad \text{if } -u + \sum_{k=0}^{n-1} f(S^k(\omega)) \leqq t < -u + \sum_{k=0}^{n} f(S^k(\omega)), \; n = 1, 2, \ldots, \\
&= (S^{-n}(\omega), u + t + f(S^{-1}(\omega)) + \ldots + f(S^{-n}(\omega))), \\
&\quad \text{if } -u - \sum_{k=1}^{n} f(S^{-k}(\omega)) \leqq t < -u - \sum_{k=1}^{n-1} f(S^{-k}(\omega)), \; n = 1, 2, \ldots,
\end{aligned}
$$

is called a *flow built under a function*. $f(\omega)$ is called the ceiling function, Ω and S are called the *base space* and the *base transformation*, respectively.

5. It was proved by W. Ambrose[4] that every ergodic measurable flow (defined on an arbitrary measure space) is isomorphic to a flow built under a function. Later it was shown[5] that the same thing is true for general non-ergotic measurable flows (defined on a measure space having a separating sequence of measurable sets) if we permit that the base space has an infinite

measure. More precisely speaking, *given a measurable flow* $\{T_t\}$ *defined on a measure space* $\Omega(\mathfrak{B}, m)$ *having a separating sequence of measurable sets, it is possible to decompose* Ω *into a countable number of disjoint invariant measurable sets:* $\Omega = \sum_{n=0}^{\infty} \Omega_n$ *(some of the terms may be missing) in such a way that (i)* $\{T_t\}$ *is the identity on* Ω_0, *and (ii)* $\{T_t\}$ *is isomorphic to a flow built under a function on each* Ω_n $(n = 1, 2, \ldots)$.

Thus the proof of Theorem 1 is reduced to the discussion of the special cases (i) and (ii). Since the first case can be easily discussed,[6] we shall discuss only the second case. Hence, from now on, we assume that $\{T_t\}$ is a flow built under a function, and we adopt the notation of section 4.

6. By assumption, there exists a constant $c > 0$ such that $f(\omega) \geqq c$ for all $\omega \in \Omega$. We may also assume that $f(\omega) \leqq 2c$ for all $\omega \in \Omega$. Next we remark that the base space $\Omega(\mathfrak{B}, m)$ is properly separable and has a separating sequence of measurable sets.[7] Let $\mathfrak{F} = \{M_n\}$ $(n = 1, 2, \ldots)$ be a basis of $\Omega(\mathfrak{B}, m)$ which is at the same time a separating sequence. We may assume that $\mathfrak{F}$ contains all sets M of the form: $M = [\omega: a \leqq f(\omega) < b]$, where a and b are arbitrary rational numbers. Further we may assume that $\mathfrak{F}$ is invariant under the base transformation S (i.e., $M \in \mathfrak{F}$ implies $S(M) \in \mathfrak{F}$ and $S^{-1}(M) \in \mathfrak{F}$). Finally, we may assume that $\mathfrak{F}$ is a finite field.

Let us now define the distance of two points ω and ω' of Ω by $d(\omega, \omega') = \sum_{n=1}^{\infty} 3^{-n} \left| \varphi_n(\omega) - \varphi_n(\omega') \right|$, where $\varphi_n(\omega)$ is the characteristic function of M_n. It is easy to see that, with respect to this metric, Ω is a zero-dimensional separable metric space and that the ceiling function $f(\omega)$ is a continuous function. Moreover, $\omega' = S(\omega)$ is a homeomorphism of Ω onto itself, and the following conditions are satisfied:

(1) every open set (and hence every Borel set) is measurable,

(2) every measurable set is contained in a Borel set of the same measure.

Let us consider the set $\bar{\Omega}^0$ of all points $\bar{\omega}$ of the form: $\bar{\omega} = (\omega, u)$, $\omega \in \Omega$, $0 \leqq u \leqq f(\omega)$, and define the distance of two points $\bar{\omega} = (\omega, u)$ and $\bar{\omega}' = (\omega', u')$ of $\bar{\Omega}^0$ by $\bar{d}(\bar{\omega}, \bar{\omega}') = d(\omega, \omega') + |u - u'|$. Then $\bar{\Omega}^0$ is clearly a one-dimensional separable metric space. If we identify two points $(\omega, f(\omega))$ and $(S(\omega), 0)$ of $\bar{\Omega}^0$ for each $\omega \in \Omega$, then we have a new metric space. This may be observed as a metrization of $\bar{\Omega}$, and it is not difficult to see that, with respect to this metrization, $\bar{\Omega}$ is a one-dimensional separable metric space, on which $\{T_t\}$ is a continuous flow. It is also not difficult to see that the conditions (1) and (2) are satisfied by the measure space $\bar{\Omega}(\bar{\mathfrak{B}}, \bar{m})$. Moreover, by assumption,

(3) every point is of measure zero;

but it is not necessarily true that

(4) every open set is of positive measure.

Let $\overline{N}$ be the union of all open sets of zero measure of $\bar{\Omega}$, if there are any. Then $\overline{N}$ is an invariant null set of measure zero, and the remaining part $\bar{\Omega} - \overline{N}$ clearly satisfies the conditions (1), (2), (3) and (4). Hence we may assume that $\bar{\Omega}$ itself satisfies all these conditions.

7. By a well-known theorem,[8] we can embed $\bar{\Omega}$ homeomorphically into a bounded part of a Euclidean 3-space R^3, and thus we obtain a representation of the given flow as a continuous flow defined on a subset of R^3. The proof of our theorem, however, is not yet finished since the measure space $\bar{\Omega}(\overline{\mathfrak{B}}, \overline{m})$, thus embedded into R^3, does not necessarily coincide with the Lebesgue* measure space $\bar{\Omega}(\mathfrak{L}^*(\bar{\Omega}), \mu^*)$.

Let $\bar{\Omega}^*$ be a bounded Borel set of R^3 such that $\bar{\Omega} \subset \bar{\Omega}^*$ and $\mu^*(\bar{\Omega}) = \mu(\bar{\Omega}^*)$, where μ and μ^* mean Lebesgue and Lebesgue outer measures in R^3. Let Q be a closed cube in R^3 which contains $\bar{\Omega}^*$ entirely in its interior, and let $\overline{\mathfrak{B}}^*$ be the collection of all subsets M of Q such that $M \cdot \bar{\Omega} \in \overline{\mathfrak{B}}$ and $M - M \cdot \bar{\Omega}^*$ is Lebesgue measurable. $\overline{\mathfrak{B}}^*$ is clearly a Borel field, and if we put $\nu(M) = \overline{m}(M \cdot \bar{\Omega}) + \mu(M - M \cdot \bar{\Omega}^*)$, then $\nu(M)$ is a countably additive completed measure defined on $\overline{\mathfrak{B}}^*$. It is clear that the condition (1) is satisfied by the measure space $Q(\overline{\mathfrak{B}}^*, \nu)$, but the condition (2) is not necessarily satisfied.

Let $\overline{\mathfrak{B}}^{**}$ be the collection of all subsets Λ of Q such that there exist two Borel sets Λ_1 and Λ_2 with $\Lambda_1 \subset \Lambda \subset \Lambda_2 \subset Q$ and $\nu(\Lambda_1) = \nu(\Lambda) = \nu(\Lambda_2)$. Then $\overline{\mathfrak{B}}^{**}$ is a Borel subfield of $\overline{\mathfrak{B}}^*$, and the measure space $Q(\overline{\mathfrak{B}}^{**}, \nu)$ clearly satisfies the conditions (1) and (2). Since the conditions (3) and (4) are clearly satisfied by the measure space $Q(\overline{\mathfrak{B}}^{**}, \nu)$, and since the boundary of Q is a set of ν-measure zero, there exists, by a theorem of J. C. Oxtoby-S. M. Ulam[9] and J. von Neumann, a homeomorphism $\omega' = h(\omega)$ of Q onto another closed cube R, which carries the measure space $Q(\overline{\mathfrak{B}}^{**}, \nu)$ into the Lebesgue measure space $R(\mathfrak{L}(R), \mu)$.

Since $Q(\overline{\mathfrak{B}}^*, \nu)$ is an extension of $Q(\overline{\mathfrak{B}}^{**}, \nu)$, it will be carried over by this homeomorphism $\omega' = h(\omega)$ into a measure space which is an extension of the Lebesgue measure space $R(\mathfrak{L}(R), \mu)$. We denote this measure space by $R(\overline{\mathfrak{L}}(R), \bar{\mu})$, where $\bar{\mu}$ is an extension of the ordinary Lebesgue measure defined on a Borel field $\overline{\mathfrak{L}}(R)$ containing all Lebesgue measurable subsets of R. Let $\bar{\Omega}' = h(\bar{\Omega})$ be the image of $\bar{\Omega}$ by $h(\omega)$, and let us consider the part of $R(\overline{\mathfrak{L}}(R), \bar{\mu})$ restricted on $\bar{\Omega}'$, which we shall denote by $\bar{\Omega}'(\overline{\mathfrak{L}}(\bar{\Omega}'), \bar{\mu})$. Since it is clear that the measure space $\bar{\Omega}'(\overline{\mathfrak{L}}'(\bar{\Omega}'), \bar{\mu})$ is isomorphic to the given measure space $\bar{\Omega}(\overline{\mathfrak{B}}, \overline{m})$, the proof of our theorem will be finished if we can prove that $\bar{\Omega}'(\overline{\mathfrak{L}}(\bar{\Omega}'), \bar{\mu})$ is the same measure space as the Lebesgue* measure space $\bar{\Omega}'(\mathfrak{L}^*(\bar{\Omega}'), \mu^*)$.

For this purpose, let $M' \in \mathfrak{L}^*(\bar{\Omega}')$. Then, by definition, there exists a Lebesgue measurable set Λ' such that $M' = \Lambda' \cdot \bar{\Omega}'$. We may assume that $\Lambda' \subset \bar{\Omega}^{*\prime} = h(\bar{\Omega}^*)$, and $\mu^*(M') = \mu(\Lambda')$. Let Λ_1' and Λ_2' be two Borel sets such that $\Lambda_1' \subset \Lambda' \subset \Lambda_2' \subset \bar{\Omega}^{*\prime}$ and $\mu(\Lambda_1') = \mu(\Lambda') = \mu(\Lambda_2')$. Let further M, Λ_1, Λ and Λ_2 be the inverse images of M', Λ_1', Λ' and Λ_2' by $h(\omega)$. Λ_1 and Λ_2

are Borel sets, and we have $\nu(\Lambda_1 - \Lambda_2) = 0$ since $\mu(\Lambda_1' - \Lambda_2') = 0$. Since $\Lambda_1 \subset \Lambda \subset \Lambda_2$, we have $\Lambda \in \overline{\mathfrak{B}}^{**}$, and consequently $M = \Lambda \cdot \bar{\Omega} \in \mathfrak{B}^*$, which in turn implies that $M' \equiv h(M) \in \bar{\mathfrak{L}}(\bar{\Omega}')$. Thus we have proved that $\mathfrak{L}^*(\bar{\Omega}') \subset \bar{\mathfrak{L}}(\bar{\Omega}')$. Moreover, we have $\mu^*(M') = \mu(\Lambda') = \nu(\Lambda) \geqq \nu(M) = \bar{m}(M) = \bar{\mu}(M')$.

Conversely, let $M' \in \bar{\mathfrak{L}}(\bar{\Omega}')$. Then there exists an $M \subset \Omega$ such that $M' = h(M)$ and $M \in \overline{\mathfrak{B}}^*$. Since $M \subset \bar{\Omega}$, we must have $M \in \overline{\mathfrak{B}}$. Hence there exist two Borel sets Λ_1 and Λ_2 such that $\Lambda_1 \cdot \bar{\Omega} \subset M \subset \Lambda_2 \cdot \bar{\Omega}$ and $\bar{m}(\Lambda_1 \cdot \bar{\Omega}) = \bar{m}(M) = \bar{m}(\Lambda_2 \cdot \bar{\Omega})$. We may assume that $\Lambda_1 \subset \Lambda_2 \subset \bar{\Omega}^*$. Let Λ be an arbitrary set such that $\Lambda_1 \subset \Lambda \subset \Lambda_2$ and $M = \Lambda \cdot \bar{\Omega}$. Let further Λ_1', Λ' and Λ_2' be the images of Λ_1, Λ and Λ_2 by $h(\omega)$. Then Λ_1' and Λ_2' are Borel sets, and, since $\nu(\Lambda_2 - \Lambda_1) = \bar{m}((\Lambda_2 - \Lambda_1) \cdot \bar{\Omega}) = 0$, we have $\mu(\Lambda_2' - \Lambda_1') = 0$. Since $\Lambda' \subset \Lambda' \subset \Lambda'$, we have $\Lambda' \in \mathfrak{L}(Q)$, which together with the relation $M' = \Lambda' \cdot \bar{\Omega}'$ will imply $M' \in \mathfrak{L}^*(\bar{\Omega}')$. Thus we have proved that $\bar{\mathfrak{L}}(\bar{\Omega}') \subset \mathfrak{L}^*(\bar{\Omega}')$. Moreover, we have $\bar{\mu}(M') = \bar{m}(M) = \nu(\Lambda) = \mu(\Lambda') \geqq \mu^*(M')$. Combined with the inequality obtained above, this will give $\bar{\mu}(M') = \mu^*(M')$ for all $M' \in \bar{\mathfrak{L}}(\bar{\Omega}') = \mathfrak{L}^*(\bar{\Omega}')$, and the proof of $\bar{\Omega}'(\bar{\mathfrak{L}}(\bar{\Omega}'), \bar{\mu}) = \bar{\Omega}'(\mathfrak{L}^*(\bar{\Omega}'), \mu^*)$ is completed.

8. In order to prove Theorem 2, we need only prove the following[10]:

LEMMA. *If a Lebesgue* measure space* $\Omega^*(\mathfrak{L}^*(\Omega^*), \mu^*)$ *in* $R^m (m \geqq 1)$ *is isomorphic to a Lebesgue measure space* $\Omega(\mathfrak{L}(\Omega), \mu)$ *in* R^n $(n \geqq 1)$, *then* Ω^* *is a Lebesgue measurable subset of* R^m.

Proof. Let $\omega^* = \varphi(\omega)$ be a measure preserving transformation of $\Omega(\mathfrak{L}(\Omega), \mu)$ onto $\Omega^*(\mathfrak{L}^*(\Omega^*), \mu^*)$ which gives this isomorphism. $\varphi(\omega)$ is clearly Lebesgue measurable. Hence there exists a Borel measurable mapping $\psi(\omega)$ such that $\varphi(\omega) = \psi(\omega)$ almost everywhere on Ω. Let Ω_0 be a Borel set such that $\Omega_0 \subset \Omega$, $\mu(\Omega - \Omega_0) = 0$ and $\varphi(\omega) = \psi(\omega)$ everywhere on Ω_0. Then $\Omega^* = \varphi(\Omega) = \varphi(\Omega_0) + \varphi(\Omega - \Omega_0) = \psi(\Omega_0) + \varphi(\Omega - \Omega_0)$. Since $\psi(\Omega_0)$ is Lebesgue measurable as the image of a Borel set Ω_0 by a Borel measurable mapping $\psi(\omega)$, and since $\varphi(\Omega - \Omega_0)$ is of Lebesgue measure zero as the image of a set of measure zero $\Omega - \Omega_0$ by a measure preserving transformation $\varphi(\omega)$, Ω^* must be measurable.

[1] For details of definition, see Ambrose, W., and Kakutani, S., "Structure and Continuity of Measurable Flows," to appear in *Duke Math. Jour.* The author is much indebted to Dr. W. Ambrose for his kind conversations on the subjects discussed in the present paper.

[2] See Doob, J. L., "Stochastic Process Depending on a Continuous Parameter," *Trans. Amer. Math. Soc.*, **42**, 107–140 (1937).

[3] See Ambrose, W., "Representation of Ergodic Flows," *Ann. Math.*, **42**, 723–739 (1941).

[4] See reference 3 above.

[5] See reference 1 above.

[6] In this case, we have only to prove that every properly separable measure space, which has a separating sequence of measurable sets and on which every point is of mea-

sure zero, is isomorphic to a Lesbesgue* measure space in R^3. We can even prove that such a measure space is isomorphic to a Lebesgue* measure space in R^1.

[7] See reference 1 above, Lemmas 5 and 6.

[8] This embedding can be carried out in a concrete way. First we map the base space Ω onto a zero-dimensional set X in the interval $0 \leqq x \leqq 1$ by $x = \Sigma 3^{-n}\phi_n(\omega)$, where $\phi_n(\omega)$ is the characteristic function of M_n. Then $\bar{\Omega}^0$ can be considered as a set in the (x, u)-plane. The final embedding of $\bar{\Omega}$ into R^3 can be obtained by twisting $\bar{\Omega}^0$ in R^3 and by identifying the points which correspond to $(\omega, f(\omega))$ and $(S(\omega), 0)$.

[9] Oxtoby, J. C., and Ulam, S. M., "Measure Preserving Homeomorphism and Metrical Transitivity," *Ann. Math.*, **42**, 874–920 (1941). Theorem 2_1.

[10] Theorem 2 is also true if the given measure space $\Omega(\mathfrak{B}, m)$ is normal in the sense of Halmos, P., and von Neumann, J., *Bull. Amer. Math. Soc.*, **47**, 696–697 (1941).

INVERSION OF A GENERALIZED LAPLACE INTEGRAL

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The transform

$$f(z) = \left(\frac{2z}{\pi}\right)^{1/2} \int_0^\infty t^{1/2} K_\nu(zt)\, d\alpha(t), \tag{1}$$

in which $K_\nu(x)$ denotes a Bessel function of imaginary argument,[1] has recently been discussed by C. S. Meijer[2] and R. E. Greenwood.[3] This transform is a generalization of the Laplace transform, to which it reduces when $\nu = \pm 1/2$. Meijer obtained an inversion formula for (1) generalizing the complex inversion formula for Laplace transforms. The object of this note is to point out that (1) can also be inverted by means of a differential operator which is a generalization of the Post-Widder inversion operator[4] for Laplace transforms. In addition, necessary and sufficient conditions for the representation of a given function $f(z)$ in the form (1) can be expressed in terms of the inversion operator.[5]

Let us define differential operators W, Q_k, by the relations

$$W[g(z)] = z^{2\nu - 1}[z^{1-2\nu} g'(z)]',$$

$$Q_k[f(u)] = \frac{1}{(2k)!}\left(\frac{2k}{u}\right)^{2k + 3/2 - \nu} W^k[z^{\nu - 1/2} f(z)]\Big|_{z = 2k/u}.$$

We suppose that $-1/2 < \Re(\nu) < 1/2$, and that (1) converges for some z (and hence for any z' with larger real part).

THEOREM 1. *If $\alpha(t)$ is the indefinite integral of $\varphi(u)$, then for almost all positive u*

$$\varphi(u) = \lim_{k \to \infty} Q_k[f(u)]. \tag{2}$$

THEOREM 2. *If $\alpha(t)$ is a function of bounded variation on every finite interval, then for all positive t*

$$\frac{\alpha(t+) + \alpha(t-)}{2} - \alpha(0+) = \lim_{k \to \infty} \int_0^t Q_k[f(u)]du.$$

THEOREM 3. *The function $f(z)$ has the representation (1) with $\alpha(t)$ the integral of a bounded function if and only if $f(x)$ is of class C^∞ on $(0, \infty)$, $f(\infty) = 0$, and*

$$| Q_k[f(u)] | \leqq M \ (0 < u < \infty; \ k = 1, 2, \ldots).$$

Other representation theorems, resembling known theorems for Laplace transforms,[6] can also be proved. However, it seems unlikely that $Q_k[f(u)] \geqq 0$ is either necessary or sufficient for (1) with increasing $\alpha(t)$, if ν is not real.

Proofs of Theorems 1 and 3 will now be sketched.

LEMMA. *If $\varphi(u)$ is integrable on every finite interval and $\int_0 \varphi(u)du = O(e^{ct})$ for some c, then the integrals*

$$I_k(u) = \left(\frac{2}{\pi}\right)^{1/2} \frac{(2k)^{2k+3/2}}{(2k)!} \int_0^\infty y^{2k+1/2} K_\nu(2ky)\varphi(uy)dy$$

exist for sufficiently large k, and $\lim_{k \to \infty} I_k(u) = \varphi(u)$ for almost all positive u, including all points of continuity of $\varphi(u)$.

The hypotheses of the lemma are easily verified if (1) converges with $(\alpha t) = \int_0 \varphi(u)du$. It is known[7] that for almost all positive u

$$\lim_{n \to \infty} \frac{n^{n+1}}{n!} \int_0^\infty y^n e^{-ny} \{\varphi(uy) - \varphi(u)\} dy = 0. \tag{4}$$

The lemma is proved by combining (4) with estimates furnished by the asymptotic expansion[8] of $K_\nu(x)$.

From the elementary properties[9] of $K_\nu(x)$ we find that

$$W_z[z^\nu K_\nu(zt)] = t^2 z^\nu K_\nu(zt). \tag{5}$$

It is easy to see that if (1) converges, the derivatives of $f(z)$ may be evaluated by differentiation under the integral sign. It is found, using (5), that

$$W^k[z^{\nu-1/2} f(z)] = z^\nu \left(\frac{2}{\pi}\right)^{1/2} \int_0^\infty t^{2k+1/2} K_\nu(zt) d\alpha(t).$$

If $\alpha(t)$ is the indefinite integral of $\varphi(t)$, the change of variable $t = uy$ leads to the result that

$$Q_k[f(u)] = I_k(u);$$

Theorem 1 now follows from the lemma.

The necessity of (3) for Theorem 3 is established similarly. To prove the sufficiency, let (3) be satisfied and consider

$$J_k(x) = \left(\frac{2x}{\pi}\right)^{1/2} \int_0^\infty t^{1/2} K_\nu(xt) Q_k[f(t)]\,dt.$$

The change of variable $u = 2k/t$ reduces this to

$$J_k(x) = \frac{1}{(2k-1)!}\left(\frac{2kx}{\pi}\right)^{1/2} \int_0^\infty u^{-1} K_\nu(2kx/u)\, V_k[u^{-1/2} f(u)]\,du,$$

where

$$V_k[g(u)] = u^{2k-\nu} W_k[u^\nu g(u)]. \tag{6}$$

It is easily verified that V_k is an Euler operator.[10] If $\overline{V}_k$ denotes the adjoint of V_k, we then have[11]

$$J_k(x) = \frac{1}{(2k-1)!}\left(\frac{2kx}{\pi}\right)^{1/2} \int_0^\infty u^{-1/2} f(u)\, \overline{V}_{k,u}\,[u^{-1} K_\nu(2kx/u)]\,du, \tag{7}$$

where $\overline{V}_{k,u}$ operates with respect to u, provided that

$$u^{p+q+1} \frac{d^p}{du^p}\,[u^{-1/2} f(u)]\, \frac{\partial^q}{\partial u^q}\,[u^{-1} K_\nu(2kx/u)] \to 0 \tag{8}$$

as $u \to 0$ and $u \to \infty$, for $p, q = 0, 1, 2, \ldots, 2k-1$. Now the hypothesis of Theorem 3 implies in particular that $g(u) = u^{-1/2} f(u)$ satisfies

$$g(u) = o(u^{-1/2}),\ V_k[g(u)] = O(u^{-3/2}) \quad (u \to \infty).$$

By a theorem of the author[12] these relations imply that

$$g^{(p)}(u) = o(u^{-p-1/2}) \quad (u \to \infty;\ p = 1, 2, \ldots, 2k-1).$$

The function $h(u) = u^{-1} K_\nu(2kx/u)$ satisfies

$$h^{(q)}(u) = O(u^{-q-1/2}) \quad (u \to \infty),$$

as may be shown, for example, by another application of the same theorem, using (9) (below). Similar reasoning applies when $u \to 0$, and we obtain (8) and consequently (7). But $u^{-1} K_\nu(2kx/u)$ is homogeneous of order -1, and hence[13]

$$\overline{V}_{k,u}\,[u^{-1} K_\nu(2kx/u)] = V_{k,x}\,[u^{-1} K_\nu(2kx/u)]. \tag{9}$$

We find, then, using (5) and (6), that

$$\begin{aligned} J_k(x) &= \frac{1}{(2k-1)!}\left(\frac{2kx}{\pi}\right)^{1/2} \int^\infty u^{-3/2} f(u) \left(\frac{2kx}{u}\right)^{2k} K_\nu\left(\frac{2kx}{u}\right) du \\ &= \left(\frac{2}{\pi}\right)^{1/2} \frac{(2k)^{2k+3/2}}{(2k)!} \int_0^\infty t^{2k+1/2} f\left(\frac{x}{t}\right) K_\nu(2kt)\,dt. \end{aligned}$$

By the lemma,

$$J_k(x) \to f(x) \quad (k \to \infty).$$

It is now easy to complete the proof along standard lines.[14]

[1] Watson, G. N., *A Treatise on the Theory of Bessel Functions*, 1922, p. 78.

[2] Meijer, C. S., *K. Akad. v. Wetenschappen te Amsterdam, Proc. Sect. Sci.*, **43**, 599–608, 702–711 (1940).

[3] Greenwood, R. E., *Ann. Math.*, **42** (2), 778–805 (especially 804) (1941).

[4] Widder, D. V., *Trans. Amer. Math. Soc.*, **39**, 244–298 (1936); further references are given in this paper.

[5] Other representation theorems are given by Meijer, op. cit., and by the present author in a paper forthcoming in *Bull. Amer. Math. Soc.*

[6] Widder, op. cit.

[7] Widder, D. V., *Trans. Amer. Math. Soc.*, **36**, 107–200 (especially 122 ff.) (1934).

[8] Meijer, op. cit., p. 601; Watson, op. cit., p. 219.

[9] Watson, op. cit., p. 79.

[10] Boas, R. P., and Widder, D. V., *Trans. Amer. Math. Soc.*, **45**, 1–72 (especially 34) (1939).

[11] *Ibid.*, **45**, 1–72 (especially 35) (1939).

[12] Boas, R. P., *Duke Math. Jour.*, **3**, 637–646 (especially 643) (1937).

[13] Boas and Widder, op. cit., p. 37.

[14] See, e.g., Boas and Widder, op. cit., p. 58.

ON FORMAL EXPONENTIAL DIFFERENTIATION IN RINGS

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The invariantive character of the operation

$$\frac{d^n(e^{av})}{dv^n} = a^n e^{av}$$

has been taken advantage of in many algebraic and analytical connections. Much of this work has been purely formal and algebraic, not really depending on the analytic properties of the exponential function. In order to make these formal methods as convenient as possible, in many applications, the writer sets up the concepts explained in the present paper. In particular, the notion of a polynomial in which the exponents may be members of an algebraic ring, not necessarily rational, is introduced.

Let R be a commutative ring including the ring of rational integers and write formally

$$A(x) = \alpha_1 x^{a_1} + \alpha_2 x^{a_2} \ldots + \alpha_s x^{a_s} \qquad (1)$$

where the α's are in R and *also the a's, the latter not necessarily in the rational ring* and x is an indeterminate in R with $x^0 = 1$ and $1 \cdot x^a = x^a$. We shall call (1) a formal polynomial in R. If we have also

$$B(x) = \beta_1 x^{b_1} + \beta_2 x^{b_2} \ldots + \beta_t x^{b_t} \tag{2}$$

with now the a's in (1) distinct as well as the b's in (2), then

$$A(x) = B(x) \tag{3}$$

If and only if $s = t$, the b's are the a's in some order, and if $a_i = b_j$ then $\alpha_i = \beta_j$. Also, for any $A(x)$ and $B(x)$ we have

$$A(x) + B(x) = B(x) + A(x). \tag{4}$$

For multiplication of these polynomials we use the rules

$$\alpha x^a \cdot \beta x^b = \alpha\beta x^{a+b} \tag{5}$$

$$\begin{aligned}(A(x) + \alpha x^a)B(x) &= B(x)(A(x) + \alpha x^a) \\ &= A(x)B(x) + \alpha x^a B(x).\end{aligned} \tag{6}$$

The use of the last two relations will enable us to express the product of any two polynomials as a polynomial, and similarly for any number of factors. Application of (6) also gives

$$\alpha_1 x^a + \alpha_2 x^a \ldots + \alpha_n x^a = (\alpha_1 + \alpha_2 + \ldots + \alpha_n)x^a \tag{7}$$

so that it follows that any formal polynomial may be reduced to a polynomial in which all the exponents of x appearing therein are distinct.

We shall now define *formal exponential differentiation* in this system. Write, using (1),

$$\overline{D}_x A(x) = \alpha_1 a_1 x^{a_1} + \alpha_2 a_2 x^{a_2} + \ldots + \alpha_s a_s x^{a_s}. \tag{8}$$

This is said to be the *formal exponential derivative* of $A(x)$ with respect to x. Note that if any of the a's is zero the corresponding term vanishes in the derivative, corresponding to the ordinary notion that the derivative of a constant is zero. Repeated use of this formula gives the *n-th formal exponential derivative,*

$$\overline{D}_x^{(n)} A(x) = \alpha_1 a_1^n x^{a_1} + \ldots + \alpha_s a_s^n x^{a_s}. \tag{9}$$

Henceforth we shall abbreviate the left-hand member of (9) as $\overline{D}^{(n)}(A)$, as differentiation will all be with respect to x in this paper and only polynomials in x will be employed.

We may prove easily by induction the relation

$$\overline{D}^{(n)}(AB) = \sum_{i=0}^{n} \binom{n}{i} \overline{D}^{(i)}(A)\overline{D}^{(n-i)}(B), \tag{10}$$

which is the analog of the Leibniz formula. More generally, by similar methods we find

$$\overline{D}^{(j)}(A_1A_2\ldots A_s) = (A_1 + A_2 + \ldots + A_s)^j, \qquad (11)$$

where, in the expression on the right, we expand by the multinomial theorem and replace A_i^r by $A_i^{(r)}$ with $A_i^{(r)} = \overline{D}^{(r)}(A_i)$; the latter theorem is written in the form

$$(A_1 + A_2 + \ldots + A_s)^j = \frac{j!}{c_1!\, c_2!\ldots c_s!} A_1^{c_1}A_2^{c_2}\ldots A_s^{c_s}, \qquad (12)$$

the summation ranging independently over each set of positive or zero c's satisfying

$$c_1 + c_2 + \ldots + c_s = j,$$

and further $A_i^0 = A_i$.

We may introduce the quotient of two formal polynomials A/B where now all exponents are rational integers and R is a field, and handle it in a fashion similar to the way the quotient of two ordinary polynomials is treated. For the derivative of such an expression we make a definition so that if $B \neq 0$ and

$$\frac{A}{B} = C$$

then

$$\overline{D}(A) = B\overline{D}(C) + C\overline{D}(B),$$

which gives

$$\overline{D}(C) = \frac{B\overline{D}(A) - A\overline{D}(B)}{B^2}, \qquad (13)$$

after substituting A/B for C on the right.

Employing polynomials involving exponents which may not be rational, in the matter indicated above, we may prove the following theorem:

Let R be the ring of algebraic integers in an algebraic field and put

$$f_{n_i}^{(i)}(\alpha_1, \alpha_2, \ldots, \alpha_{k_i}) = \sum_{r=1}^{k_i} \alpha_{ri}a_{ri}^{n_i}$$

where the a's and α's are in R and the n's are rational integers $\geqq 0$. Further let there be a rational integer $d > 0$ such that for all r's in the range 1 to k_i and all i's in the range 1 to s,

$$a_{ri}^{\,d} \equiv 1 \pmod{\mathfrak{m}}$$

where $\mathfrak{m}$ is a fixed ideal in R. Also, let

$$\beta_1 + \beta_2 + \ldots + \beta_s \equiv 0 \pmod{\mathfrak{m}}$$

where the β's are in R and suppose that $\mathfrak{a}_i$ is the greatest common ideal divisor of the ideals

$$(a_{ri}),\ r = 1, 2, \ldots, k_i,$$

each of which has a factor, $\neq (1)$, in common with $\mathfrak{m}$, then

$$(f_{n_1} + f_{n_2} + \ldots + f_{n_s})^j \equiv 0 \pmod{(\mathfrak{m}^j, \mathfrak{a}_1, \mathfrak{a}_2, \ldots, \mathfrak{a}_s)}$$

where we expand the left-hand member employing (12), and set

$$f_{n_i}^{\ t} = \beta^t f_{n_i}^{(i)} + {}_{td}(\alpha_1, \alpha_2, \ldots, \alpha_{k_i}),$$
$$i = 1, 2, \ldots, s.$$

The proof of this follows rather closely the argument employed for the proof of a related theorem[1] given by the writer in another paper, after we introduce the generalized exponents referred to above.

The theorem of the present paper has many applications which I hope to consider elsewhere.

[1] *Bull. Amer. Math. Soc.*, **43**, 420–421 (1937).